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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/170,042	10/13/1998	GREGG HASTINGS	PF226D1	6370

22195 7590 04/01/2003

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EXAMINER	
HAYES, ROBERT CLINTON	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 04/01/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/170,042	Applicant(s) Hastings et al
	Examiner Robert C. Hayes, Ph.D.	Art Unit 1647

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jan 3, 2003*.

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *21-26, 28-49, 54-56, and 58-60* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☒ Claim(s) *28-35* is/are allowed.

6) ☒ Claim(s) *21-26, 36, 37, 43-49, 54-56, and 58-60* is/are rejected.

7) ☒ Claim(s) *38-42* is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Response to Amendment

1. The amendment filed 1/03/03 has been entered.

2. The rejection of claims 38-47 & 54-57 & 60 under 35 U.S.C. 112, first paragraph, as containing new subject matter is withdrawn due to either the amendment or cancellation of the claims, or because of Applicants' arguments.

3. The rejections of claims 50-53, 57-60 & 61 under 35 U.S.C. 112, second paragraph, are withdrawn due to either the amendment or the cancellation of the claims.

4. The rejection of claims 36, 50-53, 55, 57, 59 & 61 under 35 U.S.C. 102(b) as being anticipated by Jessell et al. (U.S. Patent 5,279,966) is withdrawn due to either the cancellation or amendment of the claims.

5. Claims 28-35 are allowed.

6. Claims 38-42 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

7. Applicants' arguments filed 1/03/03 have been considered but are not found persuasive.

8. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

9. Claims 21-26, 45, 54-56 & 58 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons made of record in Paper No: 14 (mailed 10/03/02), and as follows.

Applicants argue on pages 9-11 of the response that "the claimed polypeptide 'promotes neuronal cell adhesion or axonal neurite extension' ", that the "genus of fragments of the NAF-1 polypeptide of the invention are essentially chemical claims involving generic chemical formulas", and that "the instant claims clearly distinguish the boundaries of each claimed genus and identify all of the members of each genus", and cites *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd., Eli Lilly* and *Union Oil Co. v. Atlantic Richfield Co.* Although Applicants' arguments are persuasive for claims 36-44, 46-49 & 59-60, base claim 21 alternatively recites a "polypeptide comprising an amino acid sequence which is at least 95% identical to a member selected from the group...", in which the claims are not limited to a subgenus within SEQ ID NO:2 or to even human sequences, and in which amino acid sequences are different from

"chemical formulas" because any amino acid change results in changing the polypeptide itself, by definition. In other words, the claims still encompass undescribed molecules from different species and/or allelic variants thereof that are not limited to SEQ ID NO:2; especially as it relates to heterologous sequences fused to polypeptides that merely "consist of at least"/comprise "9/10 contiguous amino acids of SEQ ID NO:2". Nor are the population of neurons that this polypeptide putatively exerts any definable and assayable function recited in the claims, or known in the art at the time of filing the instant invention. Accordingly, consistent with that held by the court in *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993), "an adequate written description of a DNA [product] requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself". *Fiddes v. Baird*, 30 USPQ2d 1481, 1483 (1993) held that claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class, in which the specification had provided an adequate description of only the bovine sequence. Similarly, only the single human NAF-1 polypeptide species of SEQ ID NO:2 has been described in the instant specification. *Univ. California v. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997) further held that:

"A description of a genus of cDNAs [products] may be achieved by means of a recitation of a representative number of cDNAs [products], *defined by nucleotide sequence*, failing in the scope of the genus or of a recitation of structural features common to the members of the genus, *which features constitute a substantial portion of the genus* [emphasis added]. This is analogous to enablement of a genus under 112, [first paragraph], by showing the enablement of a representative number of species within the genus. See Angstadt, 537 F.2d at 502-03, 190 USPQ at 218".

In contrast, an invitation for others to discover a representative number of species with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, does not reasonably show that Applicants were in possession of the claimed genus, again because only the single human NAF-1 polypeptide species of SEQ ID NO:2 is specifically described in the instant specification, and in which no distinguishable assayable function to a known population of neurons is recited in the claims. Thus, Applicants' arguments are not persuasive for the reasons made of record.

In summary, page 5 of the specification states that "NAF-1 does not appear to be the human counterpart of the rat FSP", yet the putative function for the solely described human NAF-1 polypeptide of SEQ ID NO:2 appears to be based on homology to rat FSP type 1 repeats of only 38% (e.g., see pg. 5 of the specification); thereby, providing no adequate written description of what constitutes any different species, allelic variant (i.e., as both encompassed by the recitation of "at least 95%), or different open reading frame that merely "consist at least of"/comprise generic heterologous polypeptides fused to random fragments of SEQ ID NO:2.

Applicant is again directed toward the Revised Interim Utility and Written Description Guidelines, Federal Register, Vol.64, No.244, pages 71427-71440, Tuesday December 21, 1999. For example, see Examples 13 & 17.

10. Claims 21-26, 36-37, 43-49, 54-56 & 58-60 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the specific polypeptide depicted

as SEQ ID NO:2, does not reasonably provide enablement for any biological functional equivalent polypeptides/ fragments with little structural characterization and no distinguishable recited functional characteristics. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims, for the reasons made of record in Paper No: 14 (mailed 10/03/02), and as follows.

Applicants argue on pages 11-14 the response that they have amended the claims to recite "consisting of", and functional language, etc. In contrast to Applicants' assertions, the recitation of "consisting of *at least*..." is no different from "comprising" language, in which the current functional language further fails to recite what population of neurons this functional language is suppose to have an effect upon; thereby, not currently providing an assay by which one of "ordinary skill in the art to make and test NAF-1 polypeptide variants without undue experimentation". Moreover, in contrast to Applicants' assertions, "make and test" is not the basis of the court's decision in *In re Wands*, in which alternatively a "reasonable amount of experimentation" requires at least a minimum ability to structurally know when the skilled artisan is in possession of Applicants' invention, which further requires sufficient guidance within the specification on how to make and use the claimed invention. In contrast, not even the human NAF-1 polypeptide of SEQ ID NO:2 is actually shown to function in any specific and described assay, and only specific epitope sites have been disclosed on page 21 of the specification. Moreover, because each population of neurons express their own unique set of

receptors, and because the specification fails to disclose what population of neurons possess receptors for the NAF-1 polypeptide, or what critical amino acids within SEQ ID NO:2 are required for any given function, the current claims merely constitute an invitation for other to experiment to discover Applicants' invention, which is therefore not reasonably enabled consistent with that held by the courts in *In re Wands*.

Applicants then argue that "[a]s long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim[s], then the enablement requirement is satisfied", and cites *In re Fisher, In re Wands* and *Atlas Powder Co. v. E.I. DuPont de Nemoirs*, and the references of Klar et al., Ron et al., Dobeli et al. and Bowie et al., for which none of these references have been provided to the Office in a properly executed IDS; nor have copies been provided for the Examiner's consideration; nor are the claims limited to making only "silent mutations" as described on page 15 of the specification concerning Bowie. Additionally, the attempt to incorporate subject matter into this application by reference to Klar et al, for example, is improper because Klar is not an US patent nor US application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157, 163, 167 (CCPA 1973). Thus, the claims are clearly not commensurate in scope with the limited guidance provided within the specification where no assay can be reasonably be carried out by one of ordinary skill int he art without knowing what population of neurons bind NAF-1, or what actually constitutes a functional epitope; thereby, requiring undue experimentation to discover Applicants' invention, for the reasons made of record.

In contrast to Applicants' contentions on page 14 of the response that references (i.e., Rudinger) are not representative of the state of the art at the time of the instant invention merely due to their age is not relevant, because no documentary evidence to the contrary has been made of record, nor has any evidence been provided that teaches away from that taught by Rudinger. See *In re Wright*, 569 F.2d 1124, 193 USPQ 332 (CCPA 1977).

Lastly, in contrast to Applicants' assertions concerning "consensus functional motifs within NAF-1" on page 13 of the response as "providing extensive guidance to enable" the invention, Skolnick et al. (2000) alternatively teach that:

"Sequence-based methods for functional prediction are inadequate because of the multifunctional nature of proteins. Proteins can gain and lose function during evolution and may, indeed, have multiple functions in the cell (Box 1). Sequence-to-function methods cannot specifically identify these complexities. Inaccurarate use of sequence-to-function methods has led to significant function-annotation errors in the sequence databases". (e.g., see page 34).

In summary, because the specification does not teach which particular amino acids are critical for any NAF-1 protein's function, nor how to distinguish such from any different polypeptide sequence that possesses none of the desired functions of the instant invention, the lack of guidance provided in the specification as to what minimal structural requirements are necessary for any NAF-1 protein's function, or that are necessary for successfully generating an antibody to such, would prevent the skilled artisan from determining whether any random mutation, modification or truncation to the specific amino acid sequence of SEQ ID NO: 2 could be made which retains the desired function of the instant invention, because any random mutation, truncation or modification, especially with additional random heterologous amino acid

sequences manifested within such polypeptides would be predicted to adversely alter its biologically active 3-dimensional conformation, without requiring undue experimentation to determine otherwise. Thus, Applicants' arguments are not persuasive, for the reasons made of record.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Robert Hayes whose telephone number is (703) 305-3132. The examiner can normally be reached on Monday through Thursday, and alternate Fridays, from 8:30 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert C. Hayes, Ph.D.
March 24, 2003

GARY KUNZ
SUPERVISORY PATENT EXAMINER
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